REMARKS

Claims 1-12 are pending in this application. Claim 16 has been added. Upon entrance of this amendment, Claims 1-12 and 16 will be pending. Claims 1-12 stand rejected.

Claim Amendments

Claim 1 has been amended to recite that the macrocyclic compound is characterized by at least two nucleophilic moieties and that each of two nucleophilic moieties of the macrocyclic compound reacts with the bifunctional bridging component. Support for this amendment is found in the specification at page 8, line 15, to page 9, line 3, and page 22, lines 22 to 26. New claim 16 is directed to the process of claim 1 wherein each of the nucleophilic moieties is alkylated by a functional group of the bridging component. Support for this claim is found in the specification at page 8, line 15, to page 9, line 3. No new matter has been added.

Claim Rejections

In the Office Action dated December 15, 2006, the Examiner finally rejected Claim 1 under 35 U.S.C. § 112, first paragraph, for lack of enablement and Claims 1-12 under 35 U.S.C. § 103(a) as being obvious over WO 99/21864 ("Or"). Applicants appealed these rejections, and the Board of Patent Appeals and Interferences ("the Board") issued its Decision on Appeal on August 25, 2008. The Board reversed the rejection of Claim 1 under 35 U.S.C. § 112, first paragraph, and affirmed the rejection of Claims 1-12 under 35 U.S.C. § 103(a).

In affirming the rejection under 35 U.S.C. § 103(a), the Board stated that Or teaches a process for preparing a bridged erythromycin compound, including the use of catalysts, and noted that the Examiner had asserted that Or's process involved two different bridging components. Although Applicants argued on appeal that the method taught by Or requires additional chemical modifications to attained a bridged structure, the Board observed that the term "comprising', as recited in claim 1, allows for such additional steps. The Board concluded that Applicant's claimed process is anticipated by Or and affirmed the rejection of Claims 1-12 on this basis.

Claim 1, as amended, makes clear that both nucleophilic moieties react with the bridging component. This feature of Applicant's claimed invention is not taught by Or, which teaches macrocycle compounds having at least two reactive groups, each of which reacts with a separate bridging component. Only after each component is attached to the macrocycle are the two components joined together to form a bridge. Thus in the method of Or, the two reactive groups on the macrocycle to which the bridge is attached in the final product react with two different components, not a single bridging component as required by amended Claim 1.

Further, in the process taught by Or, one of the macrocyclic functional groups that reacts with a bridging component is not nucleophilic. The method of Or includes the reaction of a hydroxyl group of macrocyclic compound with carbonyl diimidazole to form an imidazole carboxylic ester moiety (see Or, Scheme 2, conversion of compound 9 to compound 10, and page 29, lines 5 to 8). The imidazole carboxylic ester moiety then reacts with the nucleophilic primary amine of component H_2N-$(CH_2)_m$-A-B-D-X^1 to form a carbamate (see Or, scheme 3 and page 22, lines 1 to 14). The imidazole carboxylic ester moiety is therefore ***electrophilic***, a conclusion supported by Boufi *et al.*, *Langmuir* 2008, **24**, 7309-7315, which is provided herewith as Exhibit A. Scheme 2 at page 7311 of Boufi *et al.* illustrates the reaction of a cellulosic hydroxyl group with carbonyl diimidazole to form an intermediate imidazole carboxylic ester moiety, which then reacts with a primary amine to form a carbamate. At page 7312, first column, Boufi *et al.* state that carbonyl diimidazole is a reagent that "increases the electrophilic character of the carbonyl group" (i.e., by forming an imidazole carboxylic ester group). Thus, in contrast to Applicant's claimed method, in which *two* nucleophilic groups react with the bridging component, in the process of Or, no more than *one* nucleophilic group on the macrocyclic compound reacts with a bridging component.

Thus, Or does not disclose a process in which two nucleophilic groups react with a bridging component, as Or teaches neither the reaction of two groups on the macrocyclic compound with a common bridging component, nor the reaction of two nucleophilic groups on the macrocyclic compound in the bridge-forming process. Therefore, Or does not anticipate amended claim 1 or claims 2-12 and 16, which depend from claim 1 or one

or more intervening claims. Withdrawal of the rejection of the claims on this basis is respectfully requested.

Moreover, Or does not render the process according to amended claim 1 obvious. There is no teaching or suggestion in Or of alternative processes for bridge formation. For example, Or discloses a process involving specified chemical reactions, and fails to suggest any alternative method for forming a bridge. In particular, Or fails to suggest a method for forming a bridge utilizing two nucleophilic functional groups on the macrocyclic compound.

In addition, Or fails to teach or suggest bridge formation via a single bridging component that reacts with two functional groups of the macrocyclic compound. First, all of the bridging reactions disclosed by Or involve two bridging components which are coupled to the macrocycle before they are joined to complete the bridge. Second, the two macrocyclic compound functional groups employed by Or in forming the bridge are never simultaneously present in any intermediate compound. That is, a first macrocyclic compound functional group is reacted with a first bridge component before the second macrocyclic functional group is even formed. This is shown in Or in Schemes 1, 2 and 3, at pages 34-36, and described at page 26, line 27, to page 33, line 4. In Scheme 1, compound 3 includes a 6-hydroxy group, which is reacted with an alkylating agent to form compound 4, which includes a 6–OR group. Two more transformations are then conducted on the macrocyclic compound to form Compound 6. The structure of Compound 6 in Scheme 2 makes it clear that the 6-OR group represents the first bridge component. In Scheme 2, Compound 6 undergoes a series of transformations to convert the 12-OH group to a 12-(imidazole carboxylic ester) group, forming Compound 10a or 10b. As discussed above, it is this 12-(imidazole carboxylic ester) group of Compound 10a or 10b that reacts with the second bridging component, $H_2N\text{-}(CH_2)_m\text{-}A\text{-}X^2$. One skilled in the art would not have been motivated to modify the method of Or by using a single bridging component capable of reacting with two functional groups of the macrocyclic compound, because in Or's method there is not a single intermediate macrocyclic compound that includes both of the required functional groups.

For at least the reasons discussed above, Or neither teaches nor suggests the invention set forth in amended claims 1-12 and 16. Reconsideration and withdrawal of the rejection of the claims on this basis are respectfully requested.

Conclusion

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 251-3509.

Respectfully submitted,

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